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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
GARVEY, TARA L	
ART UNIT	**PAPER NUMBER**
1636	

DATE MAILED: 11/18/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/814,703	ZHANG, YUANPENG	
	Examiner	Art Unit	
	Tara L Garvey	1636	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *30 March 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-22* is/are pending in the application.

4a) Of the above claim(s) *13-18* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-8, 11,12,19 and 22* is/are rejected.

7)☒ Claim(s) *9, 10, 20 and 21* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *3/30/2004* is/are: a)☐ accepted or b)☒ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Claims 1-22 are pending.

Election/Restrictions

Restriction to one of the following inventions is required under 35 U.S.C. 121:

I. Claims 1-12 and 19-22 drawn to method of preparing lipid particles, classified in class 435, subclass 458 and class 514, subclass 44.

II. Claims 13-18, drawn to a composition of lipid particles, classified in class 424, subclass 450.

The inventions are distinct, each from the other because of the following reasons:

Inventions of Group I and Group II are related as process of making and product made. The inventions are distinct if either or both of the following can be shown: (1) that the process as claimed can be used to make other and materially different product or (2) that the product as claimed can be made by another and materially different process (MPEP § 806.05(f)). In the instant case the lipid particles could be made by an alternative method such as by using an anionic lipid and removing the charge by changing the pH.

Because these inventions are distinct for the reasons given above and have acquired a separate status in the art as shown by their different classification, by their

recognized divergent subject matter and by a their requirement for different searches, restriction for examination purposes as indicated is proper.

During a telephone conversation with Judy Mohr on October 19, 2004 a provisional election was made without traverse to prosecute the invention of Group I, claims 1-12 and 19-22. Affirmation of this election must be made by applicant in replying to this Office action. Claims 13-18 are withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to a non-elected invention.

The examiner has required restriction between product and process claims. Where applicant elects claims directed to the product, and a product claim is subsequently found allowable, withdrawn process claims that depend from or otherwise include all the limitations of the allowable product claim will be rejoined in accordance with the provisions of MPEP § 821.04. **Process claims that depend from or otherwise include all the limitations of the patentable product** will be entered as a matter of right if the amendment is presented prior to final rejection or allowance, whichever is earlier. Amendments submitted after final rejection are governed by 37 CFR 1.116; amendments submitted after allowance are governed by 37 CFR 1.312.

In the event of rejoinder, the requirement for restriction between the product claims and the rejoined process claims will be withdrawn, and the rejoined process claims will be fully examined for patentability in accordance with 37 CFR 1.104. Thus, to be allowable, the rejoined claims must meet all criteria for patentability including the

requirements of 35 U.S.C. 101, 102, 103, and 112. Until an elected product claim is found allowable, an otherwise proper restriction requirement between product claims and process claims may be maintained. Withdrawn process claims that are not commensurate in scope with an allowed product claim will not be rejoined. See "Guidance on Treatment of Product and Process Claims in light of In re Ochiai, In re Brouwer and 35 U.S.C. § 103(b)," 1184 O.G. 86 (March 26, 1996). Additionally, in order to retain the right to rejoinder in accordance with the above policy, Applicant is advised that the process claims should be amended during prosecution either to maintain dependency on the product claims or to otherwise include the limitations of the product claims. **Failure to do so may result in a loss of the right to rejoinder.** Further, note that the prohibition against double patenting rejections of 35 U.S.C. 121 does not apply where the restriction requirement is withdrawn by the examiner before the patent issues. See MPEP § 804.01.

Drawings

The drawings are objected to because in Figure 1D the label for the ligand 72 mentioned on page 8 of the specification is not present and in Figure 2A in the last box of the flowchart, the word "leather (!?)" should be "leaflet'. Corrected drawing sheets in compliance with 37 CFR 1.121(d) are required in reply to the Office action to avoid abandonment of the application. Any amended replacement drawing sheet should include all of the figures appearing on the immediate prior version of the sheet, even if only one figure is being amended. The figure or figure number of an amended drawing

should not be labeled as "amended." If a drawing figure is to be canceled, the appropriate figure must be removed from the replacement sheet, and where necessary, the remaining figures must be renumbered and appropriate changes made to the brief description of the several views of the drawings for consistency. Additional replacement sheets may be necessary to show the renumbering of the remaining figures. The replacement sheet(s) should be labeled "Replacement Sheet" in the page header (as per 37 CFR 1.84(c)) so as not to obstruct any portion of the drawing figures. If the changes are not accepted by the examiner, the applicant will be notified and informed of any required corrective action in the next Office action. The objection to the drawings will not be held in abeyance.

Claim Objections

Claims 9, 10, 20, and 21 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-4, 6-8, 11, 12, 19 and 22 are rejected under 35 U.S.C. 102(b) as being anticipated by Semple et al (US 6,287,591).

Claim 1 is drawn to a method of preparing lipid particles comprising a charged lipid and a therapeutic agent and incubating the lipid particles under conditions to remove the charge from the external lipid leaflet. Claim 2 limits the invention of claim 1 to the lipid composition containing a cationic lipid. Claim 3 limits the invention of claim 1 to forming the lipid vesicles and complexing them with a therapeutic agent. Claim 4 limits the invention of claim 1 to incubating the lipid particles with uncharged lipid vesicles. Claims 6-8 limit the invention of claim 1 to a liposome incubated with a lipid derivatized with a hydrophilic polymer or with a phospholipid derivatized with polyethyleneglycol. Claims 11 and 12 limit the invention of claim 1 to a therapeutic agent that is a charged drug, a protein, a peptide or a nucleic acid. Claim 19 is drawn to a method of preparing lipid particles with an asymmetric charges lipid composition in its outer lipid coating prior to in vivo administration. Claim 22 limits the invention of claim 19 to incubating the lipid particles with neutral lipid vesicles.

Semple et al teaches a method for preparing a composition of lipid-encapsulated therapeutic agents by providing a lipid which can be cationic, a therapeutic agent and a second lipid such as a polyethyleneglycol-modified lipid are in a mixture and then changing the pH of the mixture to cause the neutralization of charges on the exterior surface of the lipid-encapsulated therapeutic agent particles (column 3, lines 29-58, column 9, lines 15-32 and 40-52, column 10, lines 9-26 and column 20, lines 56-64). They also teach that the lipid particle can be a liposome and that the therapeutic agents

can be a charged therapeutic agent, a nucleic acid, a protein or peptide (column 8, lines 16-27, column 9, lines 49-53 and column 18, lines 44-53). Semple et al also teach that neutral lipid particles (column 13, lines 17-23). The lipid composition produced by this method can then be administered in vivo as a treatment (column 19, lines 33-48, column 20, lines 5-34 and column 22, lines 21-64). Since the method neutralizes charges on the exterior surface of the lipid, the lipid particle produced reads on an asymmetric charged lipid composition. Thus, Semple et al teaches all that is recited in the instant claims.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1-5, 6-8, 11, 12, 19 and 22 are rejected under 35 U.S.C. 103(a) as being unpatentable over Semple et al (US 6,287,591) in view of Tardi et al (US 2003/0091621).

Claims 1-4, 6-8, 11, 12, 19 and 22 have been described previously. Claim 5 limits the invention of claim 4 to incubating the lipid particles with a lipid-polymer-ligand conjugate.

Semple et al teaches a method for preparing a composition of lipid-encapsulated therapeutic agents by providing a lipid which can be cationic, a therapeutic agent and a

second lipid such as a polyethyleneglycol-modified lipid are in a mixture and then changing the pH of the mixture to cause the neutralization of charges on the exterior surface of the lipid-encapsulated therapeutic agent particles (column 3, lines 29-58, column 9, lines 15-32 and 40-52, column 10, lines 9-26 and column 20, lines 56-64). They also teach that the lipid particle can be a liposome and that the therapeutic agents can be a charged therapeutic agent, a nucleic acid, a protein or peptide (column 8, lines 16-27, column 9, lines 49-53 and column 18, lines 44-53). Semple et al also teach that neutral lipid particles and a lipid modified with a targeting ligand can also be added to the mixture (column 13, lines 17-23 and column 21, lines 4-7). The lipid composition produced by this method can then be administered in vivo as a treatment (column 19, lines 33-48, column 20, lines 5-34 and column 22, lines 21-64). Since the method neutralizes charges on the exterior surface of the lipid, the lipid particle produced reads on an asymmetric charged lipid composition. Semple et al do not teach adding a ligand-polymer-conjugate to the lipid mixture.

Tardi et al teach modifying the lipid by including a lipid-polymer-targeting ligand conjugate (page 6, left column, third paragraph bridging to right column first paragraph).

It would have been obvious to one of ordinary skill in the art to modify the teachings of Semple et al to add a lipid-polymer-targeting ligand conjugate to the lipid mixture because Semple et al teach using a lipid-polymer conjugate or a lipid-targeting ligand conjugate to modify the lipid composition. One would have been motivated to do so in order to receive the expected benefit, as suggested by Semple et al and actually exemplified by Tardi et al, of modifying the lipid composition by only having to use one

conjugate such as a lipid-polymer-targeting ligand conjugate to increase the circulation time of the liposome and to bring the therapeutic agent to the desired site. Absent of any evidence to the contrary, there would have been reasonable expectation of success in using the lipid-polymer-targeting ligand since modifying lipids containing therapeutic agents with polymers and targeting ligands has been previously shown to work and to enhance the delivery of the agents to the desired sites.

Conclusion

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Tara L Garvey whose telephone number is (571) 272-2917. The examiner can normally be reached on Monday through Friday 9 am to 5:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Remy Yucel can be reached on (571) 272-0781. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

Patent applicants with problems or questions regarding electronic images that can be viewed in the Patent Application Information Retrieval system (PAIR) (http://pair-

direct.uspto.gov) can now contact the USPTO's Patent Electronic Business Center (Patent EBC) for assistance. Representatives are available to answer your questions daily from 6 am to midnight (EST). The toll free number is (866) 217-9197. When calling please have your application serial or patent number, the type of document you are having an image problem with, the number of pages and the specific nature of the problem. The Patent Electronic Business Center will notify applicants of the resolution of the problem within 5-7 business days. Applicants can also check PAIR to confirm that the problem has been corrected. The USPTO's Patent Electronic Business Center is a complete service center supporting all patent business on the Internet. The USPTO's PAIR system provides Internet-based access to patent application status and history information. It also enables applicants to view the scanned images of their own application file folder(s) as well as general patent information available to the public.

For all other customer support, please call the USPTO Call Center (UCC) at 800-786-9199.

Tara L Garvey
Examiner
Art Unit 1636

TLG

JAMES KETTER
PRIMARY EXAMINER